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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/507,925

07/05/2005

Jonathan B. Baell

18223

6810

7590

04/02/2008

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EXAMINER

CHANDRAKUMAR, NIZAL S

ART UNIT

PAPER NUMBER

1625

MAIL DATE

DELIVERY MODE

04/02/2008

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/507,925	<b>Applicant(s)</b> BAELL ET AL.	
	<b>Examiner</b> NIZAL S. CHANDRAKUMAR	<b>Art Unit</b> 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 11 February 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-21 is/are pending in the application.
- 4a) Of the above claim(s) 18, 19 and 21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-17 and 20 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

## DETAILED ACTION

### *Election/Restrictions*

Applicant's election with traverse of Group II in the reply filed on 02/11/2008 is acknowledged. The traversal is on the ground(s) the Restriction Requirement be withdrawn since it is not in compliance with 35 U.S.C. §§12i, 37 C.F.R. 1.141 and 1.142 and 1.499.

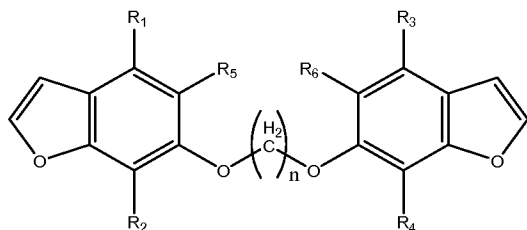
This is not found persuasive because the restriction is based on the invariable structural unit of the well known Khellinone present in claims of all the groups.

The requirement is still deemed proper and is therefore made FINAL.

Claims 18, 19 and 21 withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 02/11/2008.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

The elected Group II is  
Group 2, claim(s) 1-17, 20, drawn to compounds of formula I, wherein A=B=furan, and the linker is -O-(CH<sub>2</sub>)<sub>n</sub>-O-, and the linker and the benzofuran oxygen have meta relationship  
which corresponds to the following formula



wherein the variables are as defined in the instant claim 1.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-17, 20 drawn to the elected group of compounds are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making few of the possible structures of formula I, does not reasonably provide enablement for billions of possible structures encompassed by the formula I. For instance enablement is provided for compounds of the formula I wherein  $R1=R3=R2=R4=O\text{-alkyl}$ ,  $R5=R6=COCH3$ . However the claims are drawn to homo and heterodimers of benzofurans substituted with a wide variety of substitutions layered on top of substituents. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and **use** the invention commensurate in scope with these claims.

The determination that "undue experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the relevant factual considerations.

Enablement is considered in view of the Wands factors (MPEP 2164.01 (a)).

- 1) The breadth of the claims,
- 2) The nature of the invention,
- 3) The state of the prior art,
- 4) The level of one of ordinary skill,
- 5) The level of predictability in the art,
- 6) The amount of direction provided by the inventor,
- 7) The existence of working examples,
- 8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

While all the above factors were considered, some of the specific considerations are described below:

The nature of the invention: The invention relates to fused heterocyclic compounds that allegedly modulate potassium channel activity.

The breadth of the claims: The elected group I is drawn to compounds of the of dimeric structure wherein the substituents (layered on top of substituents) vary independently leading to homo and heterodimeric compounds of a wide variety of structure. These compounds encompass molecules that widely vary in the physical and chemical properties such as size, molecular weight, logP, acidity and basicity, properties that are known in the art to greatly influence the PK and PD parameters. Further the physical properties associated with many of the variables would render the compounds questionable candidates for blocking ion-channel of defined size and electrical properties.

The level of the skill in the art: The level of skill in the art is high. However, due to the unpredictability in the art of medicinal chemistry, it is noted that each embodiment of the invention is required to be individually assessed for viability.

The amount of direction or guidance present: The direction provided is limited and is amenable to making only few possible structures of formula I.

The direction, guidance and working examples in specification are enabling for making compounds of the elected group wherein the substituents are the same as the readily available Khellinone. Thus the direction, guidance and working examples are limited to making compounds of the formula wherein

R1=R3=R2=R4=O-alkyl, R5=R6=COCH3.

In addition, what is disclosed in the prior art as well as the in the specification relating to biological

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activity of dimeric benzofuran compounds all relate to the same substitution pattern present in Khellinone. Thus there is no structure activity relationship with respect to the substituents R1=R3=R2=R4=O-alkyl, R5=R6 except for R1=R3=R2=R4=O-CH3, R5=R6=COCH3

The specification does not provide citations (commercial or literature) for procuring the starting materials usable as per the synthetic schemes that could substitute for the lack of working examples for most if not all of the claimed variables.

The quantity of experimentation needed: In the instant case, there is a substantial gap between the guidance provided and the breadth of the claims. Given the limited direction and working Examples provided in the specification, in order to utilize the invention as claimed, the skilled artisan would be presented with an unpredictable amount of experimentation. The guidance provided in the specification is limited. Consequently, a burdensome amount of research would be required by one of ordinary skill in the art to bridge this gap.

In conclusion, based on the evidence regarding each of the above mentioned Wands factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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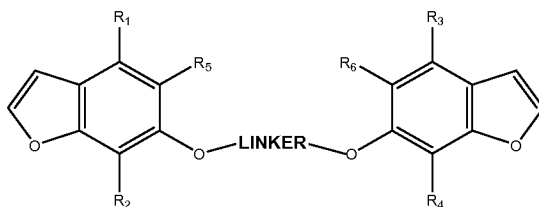
(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-17 and 20 rejected under 35 U.S.C. 103(a) as being unpatentable over Wulff et al. The Physiologist 1999, 42, p A-12.

Wulff et al. teach the well known concept of bivalent ligands for enhancing receptor potency. Specifically Wulff et al. teach the following dimeric Khellinone analogs as blockers of potassium channels.



wherein the LINKER is CH<sub>2</sub>-Ph-CH<sub>2</sub> unit, Ph being benzene and R<sub>1</sub>=R<sub>3</sub>=R<sub>2</sub>=R<sub>4</sub>=O-CH<sub>3</sub>, R<sub>5</sub>=R<sub>6</sub>=COCH<sub>3</sub> (the enabled variables of the instant case).

The only difference between the compounds of the Wulff et al, and the compounds of the instant claims is the LINKER (see above) which is alkylene chain in the instant case.

However one skilled in the art would be motivated to make analogs of Wulff et al. for use as potassium channel modulators with reasonable expectation of success because Wulff et al. teach that the biological activity resides in the Khellinone pharmacophore. The motivation to make alkyl linkers is the ready proclivity of phenols to undergo alkylation reaction, and to arrive at alternate forms of the dimeric compounds of Wulff et al. which are within the knowledge of one skilled in the art at the time of instant

application. The instantly claimed compounds would have been suggested and thus obvious to one skilled in the art.

Prior art not relied upon: Choi et al. US 6355805

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NIZAL S. CHANDRAKUMAR whose telephone number is (571)272-6202. The examiner can normally be reached on 8.30 AM - 4.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571 0272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nizal S. Chandrakumar

/D. Margaret Seaman/  
Primary Examiner, Art Unit 1625